REMARKS

Claims 1-4, 7-11, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burd et al. (US 5,939,331) in view of Killeen et al. (US 5,166,051).

Burd et al. is relied upon for teaching a test device (biosensor) that is made of plural layers of porous material having a labeling zone 26 (reagent holding part) which holds a labeled reagent for analyzing an analyte in a whole blood sample (liquid specimen having components contained therein), with said device analyzing target components in the sample by utilizing chromatography. The device further includes a matrix 23 (carrier) carrying a cell binding reagent having the ability of immobilizing cell components of said blood sample on at least a part of an area of the matrix with said area ranging from a sample (specimen) addition part to which the sample is added to a labeling zone 26. The device further includes a nitrocellulose section 27 with capture zone 29 (reaction layer) chromatographically downstream of said matrix on which a reaction between the analyte in the blood sample and the labeled reagent eluted from the labeling zone is carried out, permitting analysis of the analyte in the blood sample.

It is acknowledged that Burd et al. failed to teach that the matrix includes a cell shrinkage reagent having the ability of making the cell components of the blood sample (liquid specimen) shrink, wherein the shrunk cell components are made smaller by said cell shrinkage reagent.

In reference to Killeen et al. relied upon for teaching a diagnostic test strip for chemically determining whole blood analytes comprising a support, a porous detection zone membrane, and an overlay membrane in overlying and continuous contact with the detection zone membrane. A sample of whole blood is applied to the overlay membrane, wherein the overlay membrane contains an effective amount of a crenating agent. The crenating agent functions to deplete the volume of fluid within the red blood cells, which shrinks and rigidifies the cells, making them less flexible. The rigid cells are less able to penetrate into the pores of the detection zone membrane, which allows for the passage of analyte that has been released from the solution of the whole red blood cells into the detection zone membrane.

The rejection concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the device of Burd et al. a cell shrinking reagent within the sample addition matrix as taught by Killeen et al. because Killeen et al. teach the benefit of including a crenating (cell shrinking) reagent within a sample addition membrane, i.e. overlay membrane, of a test strip used in determining whole blood analytes because the crenating agent functions to deplete the volume of fluid within the red blood cells of a blood sample, which shrinks and rigidifies the cells, making them less flexible and less able to penetrate into the pores of the detection zone, which allows for the passage of analyte that has been released from the solution of the whole blood cells into the detection zone membrane.

With respect to claim 2, it is stated that Burd et al. teaches that the sample is whole blood.

With respect to claim 3, it is stated that Killeen et al. teaches that the liquid specimen, i.e. sample, can include bacteria.

With respect to claim 4, it is stated that Killeen et al. teach that the cell crenating (shrinkage) reagent is an inorganic salt.

With respect to claims 7 and 9, it is stated that Killeen et al. teaches that the cell crenating reagent is fried naturally or air-dried with heat.

With respect to claim 8, it is stated that Burd et al. teaches that the cell reagent applied to the sample matrix can be dried or lyophilized (freeze-dried).

With respect to claims 10 and 11, it is stated that Burd et al. teaches that the test device is a dry analytical element in the form of a one-step immunochromatographic test strip.

With respect to claim 34, it is stated that Killeen et al. teach that the crenating reagent, preferably in the form of sodium chloride should have a concentration from about 0.85 to about 35%.

On page 5 under the heading Response to Arguments it is stated that "Applicant's arguments filed April 28, 2008 have been fully considered but they are not persuasive". This conclusion is reached with respect to applicant's arguments on pages 9-14 and the submitted exhibit which conclude that Burd et al. in view of Killeen et al. would not result in applicant's invention in that it would not function without being clogged with cell pieces or carry out an immune reaction without pre-processing. On this point, the Office Action argues as follows: it is stated that applicant's appear to be arguing against the references individually and one cannot show nonobviousness by attacking references individually where the rejection is based on a combination of references.

It is further stated that Burd et al. teaches a test device (biosensor) that is made of plural layers of porous material having a labeling zone 26 which holds a labeled reagent for analyzing an analyte in a whole blood sample. The Office Action summarizes why it would have been obvious to one of ordinary skill in art at the time of the invention to modify Burd et al. with the teachings of Killeen et al. The Examiner concludes with the arguments that applicants have merely presented the merits of their application and an exhibit of blood penetration according to their invention, but do not go into detail as to why or how the combination of Burd et al. in view of Killeen et al., which would include all of the necessary structural limitations and components of applicant's invention would not function without being clogged with cell pieces.

The basic position of the Patent Office is that the Burd et al. reference includes all of the structural requirements of applicant's claimed invention except for the inclusion of a cell shrinkage reagent (i.e. crenating agent) within the carrier component. Killeen et al. provides a teaching of and motivation for including a crenating reagent within a test strip, wherein the crenating agent comprises the same compound as recited in applicants' invention i.e. an inorganic salt. The argument concludes with the statement that because the combination of Burd et al. in view of Killeen et al. results in a biosensor device of Burd et al. including the crenating agent of Killeen et al., the combination of Burd et al. in view of Killeen et al contains all of the structural limitations

and components of applicants claimed invention and provides the motivation thereof and thus renders applicants claims unpatentable and obvious.

Reconsideration and withdrawal of the above rejections are hereby requested in view of the following remarks.

The biosensor of the present application is structured such that a cell shrinkage reagent is held on at least a part of the reagent holding part or at least a part of the upstream side of the chromatographically developed part above the reagent holding part, to make the liquid sample penetrate toward the chromatographically downstream side without clogging even under conditions where the shrunk cell component is mixed into the liquid sample.

In contrast to the present invention, Killeen et al. shrinks red blood cells by extracting fluid from cells using an agent such as an inorganic salt included in the overlay membrane so as not to let the cells pass through while letting the fluid pass through, and Burd et al. removes red blood cells using a red blood cell binding reagent to provide a blood sample including no red blood cells. Accordingly, in both references the cells are removed and do not make the liquid sample penetrate toward the chromatographically downstream side without clogging even under conditions where the shrunk cell component is mixed into the liquid sample, as in the present invention. Further, Killeen et al., which makes only the fluid extracted from the red blood cells by the reagent passing through the pores of the detection zone membrane, does not teach or suggest the motivation for including the above-described reagent in the device of Burd et al. which removes the red blood cells to provide a blood sample having no red blood cells.

With respect to the issue based on the combination of the references, Applicants question the motivation or logic of combining the references. It is submitted that in view of the arguments presented above, that the objectives of the present invention cannot be accomplished even when the references are combined.

Further, the combination of Killeen et al. and Burd et al. does not result in the inclusion of all the necessary elements and the restrictions of the presently claimed invention.

As argued above, the combination of Killeen et al. and Burd et al. does not include all the constituent elements and the restrictions of the present invention, and therefore the combination fails to make a prima facie case for obviousness.

As proposed by the Examiner, supposing that Killeen et al. is combined with Burd et al., and the construction for filtration could have been used upstream in the constructions of Burd et al., multiple specimens would be required for performing the filtration, whereby the precision of measurement accuracy is deteriorated, the measurement time would be increased, the system is complicated, and an increase in cost arises, and only a device which performs filtration that is equivalent to a prior art device with its problems in the application, is obtained.

A major reason why there would be not motivation to combine the references resides in the fact that those skilled in the art have long considered it conventional to filter out the formed components in the whole blood analyte in measuring the components in blood plasma. The same can be said for the teaching of the combination of Killeen et al. and Burd et al.

In summary, note that Killeen et al. teaches that the overlay membrane contains an effective amount of a crenating agent which excludes the red blood cells from the detection zone membrane, that the red blood cells are made rigid and less flexible by being crenated, and that the red blood cells are prevented from penetrating by the ports of the detection zone membrane (column 2, lines 23-26, and lines 28-35), and that the cell components do not move to the detection zone, that is, that the “filtration” is carried out, in a manner that the formed components have been conventionally separated.

It is submitted that the combination of the references do not include all the constituent elements and restrictions of the present invention and that in the present

invention the cell components flow to the downstream as recited in the claims of the present invention.

In view of the above arguments, applicants believe that the pending application is now in condition for allowance. It is therefore requested that the above rejections be reconsidered and withdrawn, and the instant application passed to issue at an early date.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 50-0289, under Order No. 967_026RCE from which the undersigned is authorized to draw.

Dated: October 22, 2008

Respectfully submitted,

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